

# Anti-microbial Resistance and Medicinal Plants

Chelimo Faith Rebecca

Department of Clinical Medicine and Dentistry Kampala International University Uganda

Email: rebecca.chelimo@studwc.kiu.ac.ug

## ABSTRACT

Antimicrobial resistance (AMR) is a rapidly escalating global health crisis, driven by the misuse and overuse of antibiotics, poor regulation, and widespread self-medication. With resistant infections projected to cause up to 10 million deaths annually by 2050, there is an urgent need for innovative solutions. Medicinal plants, used for centuries in traditional medicine, offer promising alternatives and complementary therapies in combating resistant pathogens. This paper reviews the role of selected medicinal plants, including garlic (*Allium sativum*), turmeric (*Curcuma longa*), ginger (*Zingiber officinale*), Echinacea (*Echinacea purpurea*), and tea tree oil (*Melaleuca alternifolia*), highlighting their phytochemical properties, antimicrobial mechanisms, and evidence from clinical and laboratory studies. Key bioactive compounds such as allicin, curcumin, and gingerol demonstrate antibacterial, antifungal, antiviral, and synergistic effects when combined with conventional antibiotics. However, challenges remain in terms of dosage standardization, clinical validation, and regulatory oversight. Harnessing the therapeutic potential of medicinal plants, alongside proper stewardship of existing antibiotics, could form a sustainable and accessible strategy to slow the AMR crisis.

**Keywords:** Antimicrobial resistance, Medicinal plants, Phytochemicals, Herbal medicine, Antibiotic alternatives.

## INTRODUCTION

Currently, the world is facing the serious challenge of antimicrobial resistance. This crisis stems from the continuous increase in evolving strains of microbes that are resistant to conventional antibiotics, resulting in the ineffectiveness of numerous widely used antimicrobial drugs. Without the development of new drugs or the discovery of novel forms of treatment, this problem threatens to become even more severe. Hence, there is an urgent need for effective antimicrobial agents. Among the various options available, medicinal plants are regarded as some of the most viable alternatives for combating this escalating resistance problem. The history of human cultures is closely interwoven with the use of medicinal plants. Throughout the ages, herbal medicines have emerged as some of the oldest and most important remedies for treating numerous human diseases due to their tremendous bioactive content [1]. Currently, numerous bioactive compounds exist that are commonly used as herbal medicines, and these compounds continue to be a source of new drugs and new forms of treatment. Several plants have been studied for their antimicrobial properties and can now be part of an arsenal used to fight secondary infections and/or diseases that are difficult to treat due to their resistance to conventional antibiotics [2].

### Understanding Anti-microbial Resistance

Antimicrobial resistance is a condition arising when microorganisms develop an intrinsic ability to defeat drugs designed to kill them [1]. Microorganisms resistant to multiple drugs are often called “superbugs.” Antibiotic resistance occurs when bacteria change in response to the use of these medicines. One of the major causes of antimicrobial resistance is the misuse and overuse of antibiotics [3]. Resistance can also be intrinsic, such as the outer membrane in Gram-negative bacteria, which hinders antimicrobial penetration. Micro-organisms that are resistant to antibiotics are harder to treat, increasing the risk of disease spread and death. Antimicrobial resistance also entails serious health, social, and economic consequences on a global scale.

### Definition and Overview

Anti-microbial resistance (AMR) constitutes a global challenge that threatens the effective prevention and treatment of a growing range of infections caused by bacteria, parasites, viruses, and fungi. Known by many

popular terms, from “drug resistance” to “superbugs,” AMR is one of the broader phenomena known as “drug resistance” and is growing rapidly worldwide [2]. AMR causes regular treatment failures and requires adaptations such as greater medication doses or combinations of multiple drugs, which contribute to the negative cycle of resistance, raising serious safety concerns in health care. For example, resistance is already causing 700,000 deaths per year, poverty, famine, and extensive economic damage globally, which is challenging the principles of the modern world [2]. The overuse and misuse of prescription and non-prescription antibiotics, among other drugs, have been identified as major causes of AMR. Antibiotics are essential medicines for tackling life-threatening diseases, but they are critical to global health and sustainable development, which are both being jeopardized by the growing global resistance to antibiotics and other antimicrobials. Medicinal plants contain co-evolved blends of bioactive chemical compounds with recognized potential for reinforcing the antimicrobial activities of conventional antibiotics [2], representing an alternative possibility for addressing the AMR challenge.

### **Causes of Anti-microbial Resistance**

Anti-microbial resistance (AMR) remains a major challenge in medicine, especially in developing countries where the wide misuse and abuse of antimicrobials remain the most important cause [4]. Misuse is associated with a lack of regulation on the sale of antimicrobials and their over-the-counter availability. Such factors fuel resistances as patients often either miss doses, abandon treatment, reduce dosages, or, better still, resort to alternative treatments such as herbal remedies from traditional healers during treatment. Self-medication without proper guidance is also common and a number of herbal treatments have been shown to increase the fitness in pathogens [4]. Resistance is developed by inhibiting antimicrobial pathways. The key steps in the development of AMR are production, distribution, prescription, dispensing and consumption of drugs. Since the distribution channels in many developing countries are not well regulated, most antimicrobials can be accessed and purchased even without formal prescriptions and dispensers are mostly untrained individuals [4].

### **Global Impact of Anti-microbial Resistance**

A major global health concern, AMR renders many infectious diseases increasingly difficult and sometimes impossible to treat, requiring longer and more frequent hospital admissions and increased drug costs. Resistant microorganisms are now widespread in humans, animals, food, and the environment; AMR threatens health security and affects all pillars of global health. Patients infected by drug-resistant microorganisms are at higher risk of worse clinical outcomes and death [5]. The emergence of AMR often results from the inappropriate prescription of antibiotics, self-medication, overuse of antibiotics, and poor compliance to treatments, which can be aggravated by the lack of quick, simple, and reliable diagnostic tools. The global burden of infectious diseases is rising in part due to AMR, whose major determinants are the misuse and overuse of antibiotics in humans and animals, lack of quality assurance and surveillance, poverty, and inadequate sanitation [1].

### **An Overview of Medicinal Plants**

Medicinal plants have been used worldwide since ancient times for health and healing purposes, predominantly in rural areas where access to modern medicine was limited. In many developing countries where conventional drug supplies are scarce, medicinal plants remain the primary therapeutic agents [3]. The World Health Organization reports that, even today, approximately 80% of individuals in such countries rely on medicinal plants for health care. The interest in plant-based medicines stems from their easily accessible, affordable nature and long-standing use with minimal side effects [6]. Consequently, there has been a surge in the investigation of such plants to discover novel antimicrobial agents.

### **Historical Use of Medicinal Plants**

Historical records indicate that humans have utilized medicinal plants for thousands of years [7]. Archaeological evidence dating back to the Neanderthal Age shows the gathering of selected species, suggestive of their medicinal value. This empirical knowledge evolved into treatment practices based on aiding the body's natural healing response [7]. Early written records such as the Ebers Papyrus (~1550 BC) describe approximately 800 plant medicines, and the Hindu Vedas cite over 1,200 species. Notable historical figures such as Hippocrates and Dioscorides codified herbal remedies, creating extensive pharmacopoeias. In contemporary times, about 25% of conventional medicines incorporate plant-derived constituents or their synthetic analogues, indicating a continuing reliance on botanicals [7].

### **Current Trends in Herbal Medicine**

Historically, plants and their products have been used to treat numerous diseases among different populations and for centuries this was considered the main option for therapeutic medicine until the dawn of allopathic medicines in the twentieth century. At the beginning of the antibiotic era, people believed that antibiotics were miracle drugs and could solve many diseases; antibiotics were used indiscriminately opening the road to the development of resistance [8]. It is estimated that, annually, approximately 700,000 people die worldwide as a result of drug-resistant diseases; this number is projected to increase to 10 million by the year 2050. Since drug resistance is

increasing, it raises the length of illness and the risk of death and threatens the capabilities of modern medicine, for example, major surgery, organ transplantation and chemotherapy would become high-risk procedures [1]. Due to increasing drug resistance and the delay in the discovery of new antibiotics, the use of medicinal plants in antimicrobial treatment would be a huge benefit. Medicinal plants are a genuine gift of nature, and a valuable source of new bioactive compounds used to combat microbial infection. The efficacy of some plants used in traditional medicine is known to be genuinely related to their antimicrobial action. They are a rich source of bioactive atoms having antimicrobial, antiviral and antifungal activities. Currently, many people depend on herbal medicine as a part of primary healthcare [1]. Synergy is not a new concept in health care and it has seen resurgence in the face of increasing antimicrobial resistance. The majority of research published in the last five years reports synergy within plants and between plants and antibiotics. Whole plant extracts and combinations of compounds are more effective antimicrobials than isolated constituents of that plant. Unfortunately, many of these in vitro herbal research findings are difficult to apply to practice and are not progressing to clinical trials. To advance the field, this new body of in vitro data requires a coordinated, collaborative, innovative and interdisciplinary clinical research focus to move the synergy concept from laboratory to clinic [1, 8].

### **Mechanisms of Action of Medicinal Plants against Microbial Infections**

Medicinal plants have long been recognized for a wide spectrum of therapeutic properties, including application as alternate or complementary remedies for infectious diseases. A variety of bioactive substances (phytochemicals) contained in medicinal plants have been found to be capable of effectively acting against pathogenic microbes. Beside their direct antimicrobial action, these phytochemicals are also able to attenuate microbial resistance to available synthetic antibiotics [9]. Considerable efforts have been devoted to develop novel synthetic antibiotics. Unfortunately, rapid increase of antimicrobial resistance (AMR), coupled with a sluggish progress on the development of new synthetic antibiotics [9], has complicated the future of medicine, demanding more vigilant approaches. Medicinal plants constitute a very diverse category, among which there exist a plethora of species already known to be active against infectious diseases affecting humans [10]. This explains the recent revival of interest in medicinal plants as a viable alternative for an AMR-safe strategy. Investigations on medicinal plants have identified a number of effective modes of action. An exemplary description, according to investigations performed in the last decade, is presented below [9]. Phytochemicals may directly attack microbes by interfering with their structures such as cell wall or membrane, or functionally impair their protein or DNA synthesis, hence, leading to the arrest of cellular processes and death. Some phytochemicals show different modes of action, for instance, epigallocatechin-gallate (EGCG) inhibits bacterial efflux pumps permitting the increase of intracellular antimicrobial concentrations and, consequently, restoring the activity of synthetic antibiotics against resistant strains. A combination of synthetic antibiotics with natural substances of a different mechanism of action constitutes a synergistic mechanism since it can lead to superior efficacy and reduce potential of resistance development. On the other hand, the structural peculiarities of phytochemicals unlike synthetic antibiotics certainly provide alternative mechanisms for hinder microbial growth [9, 10].

### **Phytochemicals and Their Role**

Phytochemicals play a pivotal role in the therapeutic properties of medicinal plants. They are secondary metabolites produced by plants in response to environmental stressors, evolved primarily to protect against microbes, insects, and herbivores. These compounds have been exploited for their antimicrobial effects since antiquity and continue to underpin modern drug development. Certain phytochemicals approved for therapeutic use possess direct antimicrobial activity [2]. The emergence of antimicrobial resistance (AMR) has intensified the search for alternative treatments. Herbal medicines offer a broad array of bioactive compounds with potential against resistant infections. Whole plant extracts often display superior efficacy compared to isolated constituents, possibly due to synergistic interactions involving multiple modes of action [11]. Combining phytochemicals with conventional antibiotics can further enhance effectiveness, helping to mitigate the spread of resistant pathogens. Herbal medicines generally induce fewer adverse effects, and their phytochemical constituents seldom engender resistance. The multifaceted mechanisms of phytochemical action include perturbations of bacterial membrane permeability, efflux pump inhibition, quorum sensing disruption, and biofilm formation blockade, all critical factors in microbial survival and resistance. The capacity of phytochemicals to interfere simultaneously with diverse cellular targets affords them therapeutic promise where synthetic drugs have proven inadequate. Ongoing efforts seek to develop phytochemical-based antimicrobials, positioning plants as an invaluable resource for addressing the global AMR crisis [2, 11].

### **Synergistic Effects with Conventional Antibiotics**

Medicinal plants and conventional antibiotics can operate synergistically, potentiating antimicrobial efficacy a valuable asset in combatting multidrug-resistant microbial infections. Experimental evidence of such synergy has emerged for a number of medicinal plants in combination with diverse conventional antibiotics. Methanolic extracts of *Acacia mearnsii*, for example, exert synergistic antibacterial effects when combined with antibiotics

against clinical multi-resistant bacteria. Incorporating these combinations into therapeutic regimens promises enhanced treatment of difficult-to-treat infections [11, 12, 13]. These findings underscore the prospects of medicinal plants as sources of resistance-modulating and chemotherapeutic agents that, in tandem with standard antibiotics, bolster antimicrobial activity [12]. Similarly, ethanolic extracts of a number of medicinal plants display both intrinsic antibacterial activity and synergistic enhancement of antibiotics such as chloramphenicol, amoxicillin, doxycycline and nitrofurantoin against *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The synergistic interactions reduce the minimal inhibitory concentrations (MIC) of the antibiotics, indicative of improved efficacy. While clinical investigations are required to establish actual utility and safety, the results highlight the potential of medicinal plant extracts to augment antibiotic efficacy and control resistant bacteria [13]. Broad antibacterial effects and antibiotic-resistance reversal can also arise from phytoextracts that promote increased bacterial cell-wall permeability, inhibit antibiotic-degrading enzymes, inactivate efflux pumps, or disrupt quorum sensing signals. Corilagin, tellimagrandin I and proanthocyanidin, for instance, amplify the potency of antibiotics including oxacillin, levofloxacin, ciprofloxacin and ampicillin through these mechanisms. Corilagin from *Arctostaphylos uva-ursi* curtails the MIC of  $\beta$ -lactam antibiotics by several orders of magnitude and inhibits penicillin-binding proteins (PBP) 2a and 4, which confer resistance to PCB-containing drugs in methicillin-resistant *Staphylococcus aureus* (MRSA). Tellimagrandin I likewise substantially reduce the MIC of ampicillin, and targets PBP4 and PBP2a in MRSA, restoring antibiotic susceptibility [14].

#### **Key Medicinal Plants with Anti-microbial Properties**

Medicinal plants have been a rich source of biological activities of medicinal importance to the human race over the ages and, arguably, our ecological system. Studies suggest that nearly 65% of the world population depends on plants as traditional medications for their primary health care needs [7, 15]. Key plants such as garlic (*Allium sativum*), turmeric (*Curcuma longa*), ginger (*Zingiber officinale*), echinacea (*Echinacea purpurea*), and tea tree oil (*Melaleuca alternifolia*) have been extensively studied for anti-microbial properties [16]. The search for pharmacologically active phytochemicals has been the focus of a sizable volume of scientific literature during the last few decades, and medicinal plants still play an important role in man's quest for new drugs. Tea tree oil, for example, is a popular essential oil that is used as an anti-microbial agent worldwide and has a wide array of anti-infective applications including anti-bacterial, anti-fungal, anti-viral, and anti-parasitic [7, 15]. The phytochemicals in medicinal plants provide protection against a wide range of disease-causing microorganisms. The bioactive components of medicinal plants exhibit antimicrobial activity that helps them to cure various diseases. Essential oils, phenols, alkaloids, lectins, and polypeptides present in these plants show antimicrobial effects against bacteria, viruses, and fungi that cause infectious diseases [16]. The antimicrobial activity of various medicinal plants applied singly or in combination has been proved effective in inhibiting antibiotic-resistant microbes. According to Mahmood Ahmad and Muhammad Wajid, "Several medicinal plants have demonstrated antimicrobial activity against various pathogens".

#### **Garlic (*Allium sativum*)**

Garlic (*Allium sativum* L.) covers at least 0.75 to 1.50 m<sup>2</sup>. The bulbs are generally harvested in summer. Formerly, garlic was thought to be a South African plant (Asia). From man's village-level cultivars, garlic is distributed over the temperate regions by plummet or by trade. Cultivars of Afghanistan, Persia, India, China, Philippines, and Egypt are often cited as basil cannons for the following regions. On the other hand, in man (not rice) cultivation family distributions, especially where climate and sex types offer far more division possibilities, there is a hint of a completely different egg [17]. The Korean "Jangwhang" and Chinese "Changpu" have proven yet unrecorded Eurasian types in the diversity study of 90 tissues. Recent Korean blood examinations show the widespread transmission of diverse, historically secondary interventions of wild distributions through Northeastern China because plants and untrained. Garlic is grown in the temperate regions in isolation but also on the hill slopes at high altitude in tropical regions (up to 3000 m). Research on steam Distillation and the Extraction of Allicin from Garlic (*Allium sativum* L.) was searched on the International Journal of Engineering and Advanced Technology (IJEAT) on July 2021 [17]. The searched data show that garlic (*Allium sativum* L.) has bactericidal and bacteriostatic activities against many Gram-positive and Gram-negative agents. The typical pungent odour and antibacterial activity of garlic extracts depend on allicin, which is produced by the enzymatic hydrolysis of alliin after cutting and crushing of the cloves. Allicin shows a broad spectrum of antibacterial activity against a wide variety of antibiotic-resistant bacterial strains. From the above literature, it is concluded that gum-free garlic extract shows better activity against tested bacteria and presents a lower minimum inhibitory concentration. It gives better efficacy than the antibiotic streptomycin, which is commonly used [17].

#### **Turmeric (*Curcuma longa*)**

Turmeric (*Curcuma longa* L.), a perennial rhizomatous herb belonging to the ginger family, has been extensively studied as a broad-spectrum antimicrobial agent [18]. In a review by Nagpal and Sood, its primary pharmacological constituents are identified as curcumin and volatile oils including  $\alpha$ -tumerone,  $\alpha$ -atlantone and

zingiberone. Curcumin, a polyphenol, accounts for 0.3% to 5.4% of the raw turmeric material that is most often employed medicinally. Owing to its non-toxic nature and effective antiseptic, anti-inflammatory, analgesic and anticarcinogenic properties, there now exist numerous traditional and potential applications, for example in the management of several oral diseases [19]. With its main bioactive compound curcumin, turmeric shows substantial synergistic potential with a range of existing antimicrobial agents and several efforts are underway to enhance its aqueous solubility and bioavailability. It acts through diverse mechanisms to inhibit or kill a broad spectrum of medically important bacteria, fungi and parasites, including *Helicobacter pylori* and malaria plasmodium. Curcumin also possesses virucidal and antiviral activity and has been used as a template molecule in the design of novel agents with improved activity to broaden its therapeutic applications [18, 19].

#### **Ginger (*Zingiber officinale*)**

Ginger (*Zingiber officinale*) is a common culinary herb originating from South-East Asia [20]. It grows as a rhizome widely used as a spice, food preservative, and a medicinal herb. The rhizome contains many compounds, including starch, volatile oil, resin, gum, and mucilage. Its bioactive compounds such as gingerols, shogaols, paradols, gingerone, eugenol, and zingerone are responsible for the herb's anti-inflammatory, antioxidant, anti-nausea, antimicrobial, and anti-cancer properties [14]. Quantitative determination of total phenolic content from different geographical origins of Zimbabwean ginger rhizomes revealed a range of 1.34 to 1.80 mg GAE/g. The total flavonoid content was found to have values between 0.33 and 0.49 mg QE/g [21]. Ginger provides strong antioxidant and anti-free-radical activities and has the potential to cure many diseases, such as inflammatory disorder, blood clotting, platelet aggregation, central nervous system disorder, diabetes, cardiovascular diseases, and obesity. The DPPH radical scavenging activity was analyzed to measure the antioxidant property of ginger extract samples and revealed a range between 45% and 61% [14].

#### **Echinacea (*Echinacea purpurea*)**

*Echinacea purpurea* (Asteraceae), a perennial medicinal herb native to central and eastern North America, is traditionally used in the prevention and treatment of common colds, respiratory infections, coughs, and inflammation [22]. The plant exhibits immunostimulatory and anti-inflammatory properties and has demonstrated additional activities, including anti-anxiety, antidepressant, cytotoxicity, and antimutagenicity. While some clinical trials support its beneficial effects without serious adverse reactions, others report side effects such as abdominal pain, angioedema, dyspnea, nausea, pruritus, rash, erythema, and urticaria. *Echinacea* also displays antioxidant, antibacterial, antiviral, and larvicidal activities [22]. Its biologically active secondary metabolites encompass alkaloids, caffeic acid derivatives, polysaccharides, and glycoproteins. Analytical techniques, notably high-performance liquid chromatography (HPLC), have been employed for the simultaneous determination of key compounds such as cichoric acid and alkaloids. Although numerous studies have confirmed the plant's pharmacological potential, the precise mechanisms underlying its effects remain incompletely understood and warrant further investigation [22].

#### **Tea Tree Oil (*Melaleuca alternifolia*)**

*Melaleuca alternifolia*, commonly known as tea tree oil, exhibits a range of antimicrobial properties well documented in traditional and modern applications [23]. The essential oil of this species demonstrates antimicrobial activity against an extensive array of bacterial and fungal species, as well as certain protozoa. It has been employed to reduce the presence of methicillin-resistant *Staphylococcus aureus* (MRSA) in clinical wounds and may also positively modulate wound-healing processes [24]. In addition to its effects on MRSA, tea tree oil shows significant activity against other multidrug-resistant (MDR) strains, including *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Escherichia coli*. Several virulence factors involved in bacterial pathogenicity appear susceptible to the oil's activity. Antimicrobial susceptibility tests reveal a marked difference in the response of clinical isolates to essential oil treatment compared with carbapenem administration; when used in combination, the oil significantly enhances antibiotic efficacy, indicating a synergistic interaction. The ultra-performance liquid chromatography (UPLC) profiles of *Melaleuca alternifolia*-derived compounds bear similarity to those of carbapenems. The essential oil of *M. alternifolia* functions both as an effective natural product with distinct antimicrobial efficacy and as an adjuvant capable of restoring susceptibility in carbapenem-resistant strains [23, 24].

#### **Research Studies on Medicinal Plants and Anti-microbial Activity**

Anthropological and ethnobotanical communities have monitored the use of vernacular phyto-therapeutics. Anti-microbial screening of Pakistani plants demonstrated significant activity against tested microorganisms. Inhibition zones measuring 14 mm or more signified high anti-microbial activity. *Acacia modesta* exhibited maximum efficacy against *Escherichia coli* and *Staphylococcus epidermidis*. *Thymus serpyllum* showed pronounced activity against *Bacillus subtilis* but was inactive against *Pseudomonas aeruginosa* and *E. coli*. *Syzygium cumini* displayed peak activity against *Staphylococcus aureus* yet lacked efficacy against *E. coli*, *P. aeruginosa*, and *B. subtilis*. *Olea ferruginea* demonstrated noteworthy activity against *S. aureus*. All tested plants were significantly active against

*S. epidermidis* and generally more effective against gram-positive than gram-negative microorganisms. Methanolic extracts outperformed aqueous extracts, with activity levels dependent on concentration [25]. Investigations have also explored phyto-extracts in traditional systems, contrasting them with modern drugs. Results highlight opportunities for future research. In vitro experiments and clinical trials affirm the antimicrobial activity of numerous plants, underscoring the need for their integration into medical practice [1].

#### **In vitro Studies**

In vitro techniques provide fundamental insights into the anti-microbial properties of medicinal plants, permitting the screening of numerous extracts and evaluation of synergistic effects with conventional drugs. Common assays include contact assays and well or disk diffusion methods [26]. The disk diffusion technique assesses the inhibitory effect of plant extracts placed on antibiotic-impregnated filter paper disks applied to inoculated culture plates. The resulting zone of inhibition around each disk signifies anti-microbial activity [27].

#### **Clinical Trials**

Herbal medicines hold significant promise for enhancing antimicrobial efficacy and mitigating resistance, but the scarcity of data from rigorous human trials limits understanding of their clinical effectiveness [1]. Recent clinical evaluations have investigated formulations containing extracts from *P. sidoides*, *Echinacea*, *C. Incanus*, *P. incarnate*, and *A. paniculata*, commonly used in treating uncomplicated upper respiratory infections and uncomplicated urinary tract infections, with positive outcomes [15]. However, the application of medicinal plants against antimicrobial resistance calls for more comprehensive studies to establish precise clinical benefits. The search for effective treatments to address infections during pandemics has led to renewed interest in medicinal plants, recognized for their therapeutic properties inherited over centuries. These plants provide a rich source of bioactive compounds for the development of novel pharmaceuticals. Medicinal plants with antimicrobial effects also exhibit antiviral, antifungal, and antiparasitic properties. Current efforts emphasize identifying plants capable of preventing or reversing antimicrobial resistance, highlighting a shift towards novel therapies and the potential fusion of traditional and modern medicine to harness collective benefits [1, 15].

#### **Comparative Studies with Conventional Drugs**

Studies have demonstrated the potential of medicinal plants as alternatives to conventional anti-microbial drugs. The aqueous and ethanol extracts of *Aristolochia indica* and *Toddalia asiatica* exhibited antibacterial activity against multidrug-resistant *Enterococcus faecalis*, with inhibition zones measuring 18 mm for *A. indica* [26]. Similarly, extracts from *Nerium sp*, *Mentha sp*, *Aloe vera*, and *Eucalyptus sp* possess antibacterial and antifungal properties comparable to those of standard antibiotics; notably, *Eucalyptus* extracts maintained significant growth inhibition at lower concentrations [28]. In Ethiopia, the majority of medicinal plants screened demonstrated substantial activity against various microbial strains, a phenomenon linked to diverse secondary metabolites [15]. These findings collectively suggest that plant extracts retain efficacy against resistant bacteria and offer promising leads in the search for new anti-microbial agents [15, 26, and 28].

#### **Challenges in Integrating Medicinal Plants into Modern Medicine**

High economic costs associated with product standardization, time scales, and political and regulatory barriers remain primary obstacles to the integration of medicinal plants into modern medicine [1]. The absence of international and national guidelines, combined with the absence of definition and composition criteria for regulated products, contributes to cautious consumer acceptance. Hence, effective planning of rules for the standardization of herbal medicines is particularly pertinent, since a considerable percentage of reproductive-age women prefer herbal products for gynecological and obstetric needs [1].

#### **Standardization and Quality Control**

Standardization is necessary for verifying drug identity and assessing quality and purity. As medicinal plants gain broader use and commercialization, the need for quality-control standards strictly intensifies [29]. Quality comprises all factors that contribute, directly or indirectly, to the safety, effectiveness, and acceptability of a product. The absence of quality controls influences drug efficacy and safety, which in turn jeopardizes consumer health. Standardization addresses issues of adulteration and therefore constitutes one of the fastest-growing research domains. Herbal products containing berries of *Myrtus communis* Linn have already undergone physicochemical and phytochemical standardization [29]. Such procedures are crucial for developing new phytotherapeutic agents for treating resistant microbial infections. Microbial contamination threatens the safety of herbal medicinal formulations, particularly those sold in areas where quality control and monitoring remain underdeveloped [30]. Microbial assessment, moreover, comprises the only approach to evaluate such contaminants directly and ensures compliance with regulatory thresholds. Despite many assurances that herbal medicines are safe, numerous products that have failed even to meet local and international specifications still reach the market; various pathogenic groups may therefore abound. An examination of selected formulations revealed that neither microbial nor physicochemical parameters exceeded acceptable levels, while the microbiological profiles generally aligned well with prevailing limits. Consequently, the products were considered

suitable, safe, and efficacious for use and therapeutic application. Legislation by the World Health Organization mandates that herbal formulations maintaining microbiological levels within stated thresholds remain indispensable [30]. The European Pharmacopoeia and the European Medicines Agency likewise stipulate clear quality requirements and safety recommendations for pharmaceutical and herbal preparations. Microbial tests are therefore routinely employed to monitor such products, prevent outbreaks, and evaluate the success of decontamination procedures. Guidelines and limitations have since been adopted by numerous regulatory authorities around the world, including national bodies such as the National Agency for Food and Drug Administration and Control [29, 30].

### Regulatory Issues

The use of herbal medicine is a global phenomenon, which is gaining increasing interest in the face of systemic antimicrobial resistance (AMR). AMR threatens to reverse many of the major achievements of modern medicine, especially in the treatment of surgical procedures and cancer chemotherapy [1]. Many researchers have rediscovered the significance of plant-derived therapeutics and their potential applications. Numerous resistance mechanisms and problems have already been described from medicinal plants and conventional antibiotics. The current major issues regarding the use of medicinal plants as antimicrobial alternatives are linked to their standards, efficacy, and regulations [1]. Developing drugs effective against Gram-negative bacteria is particularly difficult due to the challenges compounds face accumulating within the cell. The rapid rise in multidrug-resistant tuberculosis (MDR-TB) caused by resistant *Mycobacterium tuberculosis* strains is a major concern, with millions of cases worldwide and a high mortality rate [3]. Projections indicate that deaths from AMR could reach 10 million annually by 2050 if urgent action is not taken, underscoring the critical need for new antibacterial agents. Although several plant-derived antimicrobial agents have been investigated, clinical trials have been limited to a few phytochemicals and botanicals. Challenges hindering the discovery and utilization of these agents include limited sources, the risk of rediscovery, suboptimal drug metabolism and pharmacokinetics, and a lack of understanding of molecular targets. Intrinsic resistance mechanisms, such as the outer membrane in Gram-negative bacteria serving as a barrier to antimicrobial penetration, further complicate the issue [3]. Such aspects need to be addressed to recommend medicinal plants as plausible alternatives to combat AMR.

### Public Perception and Acceptance

Although a majority of the world's population relies on plant-based therapies, the modern healthcare system remains predominantly rooted in conventional therapeutics, which are increasingly plagued by challenges such as rising costs, fewer new drugs, and emerging drug resistance. The commercial success of medicinal plants has led to a proliferation of herbal products, often accompanied by questionable health claims, complicated further by declining respect for traditional practice and increased patient awareness and political pressure. The apparent competition between herbal and conventional medicine obscures the potential for their complementary use [1]. Most patients are hesitant to trust conventional medicine exclusively and prefer to concurrently seek a more 'natural,' traditional remedy, making it vital for conventional practitioners to understand herbal medicine to manage it safely and effectively with their patients. Without professional guidance, however, patients may resort to untested therapies and potentially dangerous plant medicines, which could precipitate toxicity or treatment failure under misunderstood plant-drug interactions [5]. Plants, by definition, are under less suspicion than synthetic chemicals of being toxic; additionally, cultural backgrounds, the perception of 'naturalness' as 'safety,' and relatively easy access to herbal products all contribute to patients' willingness to turn to plant medicine. Understanding modalities of therapy, including dosage and potential plant-drug interactions, is therefore critical. The prudent recipe is to utilize the substantial body of information on plant-based medicines to educate communities and develop compatible policies for their safe and effective use in contemporary society [1, 5].

### Future Directions in Research

Healthcare has drawn inspiration from herbal medicine traditions, from which humans have benefited for millennia, to develop the concept that co-evolving medicinal organisms encounter selective pressures that favour increases in diversity, adaptability and synergy. Harnessing complexity and co-evolution, *Garcinia kola* seed extract synergizes effectively with antibiotics remoxipride and midodrine against multi-drug resistant (MDR) bacterial isolates in vitro. Germander leaf extract demonstrates antimicrobial synergy with amoxicillin. Such examples suggest that herbal medicine offers insights that might be embraced by conventional medicine to meet the challenge of antimicrobial resistance; targeted, collaborative, innovative, interdisciplinary clinical research is advocated [1]. Despite rapid global expansion and the demonstrated feasibility and efficacy of conventional drugs, traditional medicine remains integral to global healthcare, with increased interest in medicinal plants offering opportunities for drug development. The escalating resistance of bacteria to antibiotics has heightened interest in plants as alternative antibiotic sources [1]. Plants provide a broad spectrum of phytochemical constituents that potentially exhibit diverse bioactivities and mechanisms of action compared with currently employed antibiotics [3] in addressing antimicrobial resistance.

### Innovative Approaches to Combat Anti-microbial Resistance

The emergence and spread of antimicrobial resistance (AMR) constitute perhaps the most urgent health problems currently facing humanity. Conventional antibiotics and other antimicrobial agents have generally been over-prescribed, misused, and applied incorrectly in many parts of the world [3]. As a result, many infections, including some diseases such as tuberculosis (TB), become more difficult to treat. Additionally, some infections, such as pneumonia, foodborne diseases, and sexually transmitted infections, are more readily transmitted and could globally lead to a spiral of rising health-care costs and increased mortality. Development of innovation and novel drug-discovery methods for agents that are active against multidrug-resistant bacteria is presently of key importance. A promising approach to overcoming such challenges involves the use of natural products, especially medicinal plants [3].

### Collaborative Efforts between Traditional and Modern Medicine

Many traditional herbal medicine systems have long fostered co-evolutionary relationships between plants and pathogens and may therefore offer valuable design principles for future antibacterial development [1]. Unlike most modern drug discovery approaches, which typically rely on identifying single agents, the combined complexity embedded within traditional herbal formulations may prove more effective at overcoming the sophisticated cell-based resistance mechanisms that bacteria have evolved. When viewed through the lens of complexity science and systems biology, medicinal plants can make direct contributions to the design of new antimicrobials with improved resilience to resistance, and also provide a source of novel compounds with unexpectedly wide therapeutic activity. Such complexity has evolved to a high degree within existing medicinal plants and offers a compelling complementary approach to modern drug discovery. Collaborative, innovative and interdisciplinary clinical research into medicinal plants is therefore urgently required to meet the challenge of AMR [1]. Greater collaboration between traditional and modern medicine, and novel scientific approaches to medicinal plants and AMR, are among many vital pathways for future research. With their diverse sources of novel bio-compatible secondary metabolites, evolved synergies both within medicinal plants and between plants and antibiotics complicate the pathways available for bacteria to evolve resistance and provide unique test-beds for pioneering approaches to antibacterial drug development. The unique philosophical and theoretical frameworks embodied in traditional medicine systems therefore also offer a rich and largely untapped source of knowledge, innovation and guidance for future differentially productive and +AMR synergistic research approaches and a possible new paradigm within which medicinal plants and drugs may be integrated and Unified [1, 31, 32].

### CONCLUSION

Antimicrobial resistance represents one of the greatest threats to global health and development, undermining decades of medical progress. While antibiotics remain essential, their overuse has created an urgent need for new strategies. Medicinal plants provide a rich source of bioactive compounds with proven antimicrobial activity, immunomodulatory effects, and the potential to work synergistically with existing antibiotics. Their accessibility and affordability make them particularly relevant in low- and middle-income countries, where the burden of AMR is highest. However, their effective deployment requires overcoming challenges of standardization, dosage validation, and regulatory integration. A future approach that combines conventional antibiotics with validated medicinal plant therapies, underpinned by strong research and policy support, offers a sustainable pathway to slowing the AMR crisis. By bridging traditional knowledge with modern science, medicinal plants can play a vital role in safeguarding global health against resistant infections.

### REFERENCES

1. Mundy L, Pendry B, Rahman M. Antimicrobial resistance and synergy in herbal medicine. *Journal of Herbal Medicine*. 2016 Jun 1;6(2):53-8.
2. Khameneh B, Eskin NM, Iranshahy M, Fazly Bazzaz BS. Phytochemicals: A promising weapon in the arsenal against antibiotic-resistant bacteria. *Antibiotics*. 2021 Aug 26;10(9):1044.
3. Berida TI, Adekunle YA, Dada-Adegbola H, Kdimy A, Roy S, Sarker SD. Plant antibacterials: The challenges and opportunities. *Heliyon*. 2024 May 30;10(10).
4. Ayukekbong JA, Ntemgwa M, Atabe AN. The threat of antimicrobial resistance in developing countries: causes and control strategies. *Antimicrobial Resistance & Infection Control*. 2017 May 15;6(1):47.
5. Iriti M, Vitalini S, Varoni EM. Humans, animals, food, and environment: One health approach against global antimicrobial resistance. *Antibiotics*. 2020 Jun 19;9(6):346.
6. Kali A. Antibiotics and bioactive natural products in treatment of methicillin-resistant *Staphylococcus aureus*: A brief review. *Pharmacognosy reviews*. 2015 Jan;9(17):29.
7. Ahmad M, Wajid M. Plants as a potential source of antimicrobial agents. *Journal of Pharmacy and Alternative Medicine*. 2013;2(3):18-25.
8. Allemailem KS. Antimicrobial potential of naturally occurring bioactive secondary metabolites. *Journal of Pharmacy and Bioallied Sciences*. 2021 Apr 1;13(2):155-62.

9. Khameneh B, Iranshahy M, Soheili V, Fazly Bazzaz BS. Review on plant antimicrobials: a mechanistic viewpoint. *Antimicrobial Resistance & Infection Control*. 2019 Jul 16;8(1):118.
10. Cuevas-Cianca SI, Romero-Castillo C, Gálvez-Romero JL, Sánchez-Arreola E, Juárez ZN, Hernández LR. Latin American plants against microorganisms. *Plants*. 2023 Nov 28;12(23):3997.
11. Soberon JR, Sgariglia MA, Sampietro DA, Quiroga EN, Vattuone MA. Antibacterial activity of plant extracts from northwestern Argentina. *Journal of Applied Microbiology*. 2007 Jun 1;102(6):1450-61.
12. Olajuyigbe OO, Afolayan AJ. Synergistic interactions of the methanolic extract of *Acacia meurnsii* De Wild. with antibiotics against bacteria of clinical relevance. *International journal of molecular sciences*. 2012 Jul 17;13(7):8915-32.
13. Jouda MM, Elbashiti T, Masad A, Albayoumi M. The antibacterial effect of some medicinal plant extracts and their synergistic effect with antibiotics. *World Journal of Pharmacy and Pharmaceutical Sciences*. 2016;5(2):23-33.
14. Dassanayake MK, Khoo TJ, An J. Antibiotic resistance modifying ability of phytoextracts in anthrax biological agent *Bacillus anthracis* and emerging superbugs: a review of synergistic mechanisms. *Annals of clinical microbiology and antimicrobials*. 2021 Dec 2;20(1):79.
15. Dubale S, Kebebe D, Zeynudin A, Abdissa N, Suleman S. Phytochemical screening and antimicrobial activity evaluation of selected medicinal plants in Ethiopia. *Journal of experimental pharmacology*. 2023 Dec 31:51-62.
16. Hossan MS, Jindal H, Maisha S, Samudi Raju C, Devi Sekaran S, Nissapatorn V, Kaharudin F, Su Yi L, Khoo TJ, Rahmatullah M, Wiart C. Antibacterial effects of 18 medicinal plants used by the Khyang tribe in Bangladesh. *Pharmaceutical biology*. 2018 Jan 1;56(1):201-8.
17. Palaksha MN, Ahmed M, Das S. Antibacterial activity of garlic extract on streptomycin-resistant *Staphylococcus aureus* and *Escherichia coli* solely and in synergism with streptomycin. *Journal of natural science, biology, and medicine*. 2010 Jul;1(1):12.
18. Paul-Chima UO, Ogenyi FC, Ugwu CN, Nnaemeka UM. Gut Microbiota-Derived Metabolites as Early Biomarkers for Childhood Obesity: A Policy Commentary from Urban African Populations. *Obesity Medicine*. 2025 Sep 4:100641.
19. Zorofchian Moghadamtousi S, Abdul Kadir H, Hassandarvish P, Tajik H, Abubakar S, Zandi K. A review on antibacterial, antiviral, and antifungal activity of curcumin. *BioMed research international*. 2014;2014(1):186864.
20. Paul-Chima UO, Nnaemeka UM, Nneoma UC. Could dysbiosis of urban air microbiota be an overlooked contributor to pediatric asthma and neurodevelopmental disorders?. *Medical Hypotheses*. 2025 Sep 12:111758.
21. Nagpal M, Sood S. Role of curcumin in systemic and oral health: An overview. *Journal of natural science, biology, and medicine*. 2013 Jan;4(1):3.
22. Sharifi-Rad M, Varoni EM, Salehi B, Sharifi-Rad J, Matthews KR, Ayatollahi SA, Kobarfard F, Ibrahim SA, Mnayer D, Zakaria ZA, Sharifi-Rad M. Plants of the genus *Zingiber* as a source of bioactive phytochemicals: From tradition to pharmacy. *Molecules*. 2017 Dec 4;22(12):2145.
23. Ahmed N, Karobari MI, Yousaf A, Mohamed RN, Arshad S, Basheer SN, Peeran SW, Noorani TY, Assiry AA, Alharbi AS, Yean CY. The antimicrobial efficacy against selective oral microbes, antioxidant activity and preliminary phytochemical screening of *Zingiber officinale*. *Infection and Drug Resistance*. 2022 Jan 1:2773-85.
24. Manayi A, Vazirian M, Saeidnia S. *Echinacea purpurea*: Pharmacology, phytochemistry and analysis methods. *Pharmacognosy reviews*. 2015 Jan;9(17):63.
25. Zhang X, Guo Y, Guo L, Jiang H, Ji Q. In vitro evaluation of antioxidant and antimicrobial activities of *Melaleuca alternifolia* essential oil. *BioMed research international*. 2018;2018(1):2396109.
26. Oliva A, Costantini S, De Angelis M, Garzoli S, Božović M, Mascellino MT, Vullo V, Ragno R. High potency of *Melaleuca alternifolia* essential oil against multi-drug resistant gram-negative bacteria and methicillin-resistant *Staphylococcus aureus*. *Molecules*. 2018 Oct 9;23(10):2584.
27. Soulaïmani B, El Hidar N, El Fakir SB, Mezrioui N, Hassani L, Abbad A. Combined antibacterial activity of essential oils extracted from *Lavandula maroccana* (Murb.), *Thymus pallidus* Batt. and *Rosmarinus officinalis* L. against antibiotic-resistant Gram-negative bacteria. *European Journal of Integrative Medicine*. 2021 Apr 1;43:101312.
28. Venkatadri B, Arunagirinathan N, Rameshkumar MR, Ramesh L, Dhanasezhian A, Agastian P. In vitro antibacterial activity of aqueous and ethanol extracts of *Aristolochia indica* and *Toddalia asiatica* against multidrug-resistant bacteria. *Indian journal of pharmaceutical sciences*. 2015 Nov;77(6):788.

29. AL-Azzawi MK, Hasan NA, Barrak MM. A review of the development of an understanding of antibiotic interactions, from mechanisms of action to novel resistance and the search for natural alternatives. *Journal of Medical Genetics and Clinical Biology*. 2024;1(6):78-102.
30. Mehta R, Dhruv S, Kaushik V, Sen KK, Khan NS, Abhishek A, Dixit AK, Tripathi VN. A comparative study of antibacterial and antifungal activities of extracts from four indigenous plants. *Bioinformation*. 2020 Mar 31;16(3):267.
31. Sumbul S, Ahmad MA, Asif M, Akhtar M, Saud I. Physicochemical and phytochemical standardization of berries of *Myrtus communis* Linn. *Journal of Pharmacy and Bioallied Sciences*. 2012 Oct 1;4(4):322-6.
32. Kanu A, Igbeneghu OA, Orafidiya LO. The organoleptic and microbial quality of some herbal medicinal products marketed in Freetown, Sierra Leone. *African Journal of Traditional, Complementary and Alternative Medicines*. 2015;12(4):1-8.

**CITE AS: Chelimo Faith Rebecca (2025). Anti-microbial Resistance and Medicinal Plants. EURASIAN EXPERIMENT JOURNAL OF MEDICINE AND MEDICAL SCIENCES, 7(1):29-38**